

WHAT IS CLAIMED IS:

- 1 1. A composition comprising a biologically active compound and a
2 transport moiety, wherein the transport moiety comprises a structure selected from the group
3 consisting of $(\text{XYZ})_n\text{Z}$, $(\text{ZY})_n\text{Z}$, $(\text{ZYY})_n\text{Z}$ and $(\text{ZYYY})_n\text{Z}$, wherein each Z is L-arginine or D-
4 arginine, and each Y is independently an amino acid that does not comprise an amidino or
5 guanidino moiety, and wherein n is an integer of from 2 to 10.

- 1 2. The composition according to claim 1, wherein each Y is
2 independently selected from the group consisting of alanine, cysteine, aspartic acid, glutamic
3 acid, phenylalanine, glycine, histidine, isoleucine, lysine, leucine, methionine, asparagine,
4 proline, glutamine, serine, threonine, valine, tryptophan, hydroxyproline, tyrosine, γ -amino
5 butyric acid, β -alanine, sarcosine and ϵ -amino caproic acid.

- 1 3. The composition according to claim 1, wherein the transport moiety
2 comprises the structure $(\text{XYZ})_n\text{Z}$, and wherein n is an integer ranging from 2 to 5.

- 1 4. The composition according to claim 1, wherein the transport moiety
2 comprises the structure $(\text{ZY})_n\text{Z}$, and wherein n is an integer ranging from 4 to 10.

- 1 5. The composition according to claim 1, wherein the transport moiety
2 comprises the structure $(\text{ZYY})_n\text{Z}$, and wherein n is an integer ranging from 4 to 10.

- 1 6. The composition according to claim 1, wherein the transport moiety
2 comprises the structure $(\text{ZYYY})_n\text{Z}$, and wherein n is an integer ranging from 4 to 10.

- 1 7. The composition according to claim 1, wherein the transport moiety is
2 attached to the biologically active compound by a linking moiety to form a conjugate.

- 1 8. The composition according to claim 1, wherein Y is a gene-encoded
2 amino acid.

- 1 9. The composition according to claim 1, wherein Y is an amino acid
2 other than a gene-encoded amino acid.

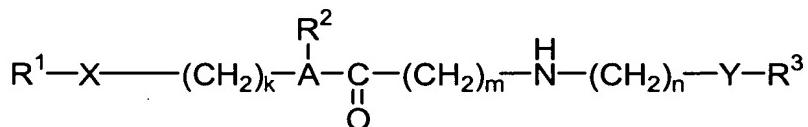
- 1 10. The composition according to claim 3, wherein each Y is
2 independently selected from the group consisting of glycine, γ -amino butyric acid, β -alanine
3 and ϵ -amino caproic acid, and n is 3 or 4.

1 **11.** The composition according to claim **4**, wherein each Y is
2 independently selected from the group consisting of glycine, γ -amino butyric acid, β -alanine
3 and ϵ -amino caproic acid, and n is 6, 7 or 8.

1 **12.** The composition according to claim **5**, wherein each Y is
2 independently selected from the group consisting of glycine, γ -amino butyric acid, β -alanine
3 and ϵ -amino caproic acid, and n is 6, 7 or 8.

1 **13.** The composition according to claim **6**, wherein each Y is
2 independently selected from the group consisting of glycine, γ -amino butyric acid, β -alanine
3 and ϵ -amino caproic acid, and n is 6, 7 or 8

1 **14.** The composition according to claim **7**, wherein the conjugate has the
2 following structure:



3 wherein:

4 **R**¹ is the biologically active compound ;

5 X is a linkage between a functional group on the biologically active compound
6 and a functional group on the linker between R¹ and R³;

7 Y is a linkage between a functional group on the transport moiety and a functional
8 group on the linker between R¹ and R³;

9 A is N or CH;

10 R² is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;

11 R³ is a transport moiety;

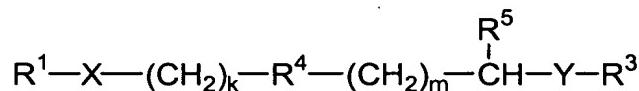
12 k and m are independently either 1 or 2; and

13 n is an integer of from 1 to 10.

1 **15.** The composition according to claim **14**, wherein each of X and Y is
2 independently selected from the group consisting of -C(O)O-, -C(O)NH-, -OC(O)NH-, -S-S-,
3 -C(S)O-, -C(S)NH-, -NHC(O)NH-, -SO₂NH-, -SONH-, phosphate, phosphonate and
4 phosphinate.

1 **16.** The composition according to claim 14, wherein each of X and Y is
2 independently selected from the group consisting of -C(O)O-, -C(O)NH-, -OC(O)NH- and
3 -NHC(O)NH-.

1 **17.** The composition according to claim 7, wherein the conjugate has the
2 following structure:



4 wherein:

5 R¹ is the biologically active compound ;

6 X is a linkage between a functional group on the biologically active compound
7 and a functional group on the linker between R¹ and R³;

8 Y is a linkage between a functional group on the transport moiety and a functional
9 group on the linker between R¹ and R³;

10 R³ is a transport moiety;

11 R⁴ is S, O, NR⁶ or CR⁷R⁸;

12 R⁵ is OH, SH or NHR⁶;

13 R⁶ is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;

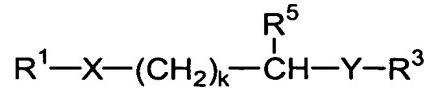
14 R⁷ and R⁸ are independently hydrogen, alkyl or arylalkyl; and

15 k and m are independently either 1 or 2.

1 **18.** The composition according to claim 17, wherein each of X and Y is
2 independently selected from the group consisting of -C(O)O-, -C(O)NH-, -OC(O)NH-, -S-S-,
3 -C(S)O-, -C(S)NH-, -NHC(O)NH-, -SO₂NH-, -SONH-, phosphate, phosphonate and
4 phosphinate.

1 **19.** The composition according to claim 17, wherein each of X and Y is
2 independently selected from the group consisting of -C(O)O-, -C(O)NH-, -OC(O)NH- and
3 -NHC(O)NH-.

1 **20.** The composition according to claim 7, wherein the conjugate has the
2 following structure:



4 wherein:

5 R¹ is the biologically active compound;

6 X is a linkage between a functional group on the biologically active compound
7 and a functional group on the linker between R¹ and R³;

8 Y is a linkage between a functional group on the transport moiety and a functional
9 group on the linker between R¹ and R³;

10 R³ is the transport moiety;

11 R⁵ is H, OH, SH or NHR⁶;

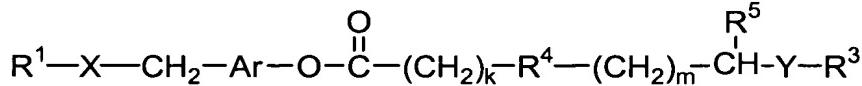
12 R⁶ is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl; and

13 k is 1 or 2.

1 21. The composition according to claim 20, wherein each of X and Y is
2 independently selected from the group consisting of -C(O)O-, -C(O)NH-, -OC(O)NH-, -S-S-,
3 -C(S)O-, -C(S)NH-, -NHC(O)NH-, -SO₂NH-, -SONH-, phosphate, phosphonate and
4 phosphinate.

1 22. The composition according to claim 20, wherein each of X and Y is
2 independently selected from the group consisting of -C(O)O-, -C(O)NH-, -OC(O)NH- and
3 -NHC(O)NH-.

1 23. The composition according to claim 7, wherein the conjugate has the
2 following structure:



4 wherein:

5 R¹ is the biologically active compound;

6 X is a linkage between a functional group on the biologically active compound
7 and a functional group on the linker between R¹ and R³;

8 Y is a linkage between a functional group on the transport moiety and a functional
9 group on the linker between R¹ and R³;

10 Ar is a substituted or unsubstituted aryl group, wherein the methylene and oxygen
11 substituents are either *ortho* or *para* to one another;

12 R³ is the transport moiety;

13 R⁴ is S, O, NR⁶ or CR⁷R⁸;

14 R⁵ is H, OH, SH, CONHR⁶ or NHR⁶;

15 R⁶ is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;
16 R⁷ and R⁸ are independently hydrogen or alkyl; and,
17 k and m are independently either 1 or 2.

1 **24.** The composition according to claim 23, wherein each of X and Y is
2 independently selected from the group consisting of -C(O)O-, -C(O)NH-, -OC(O)NH-, -S-S-,
3 -C(S)O-, -C(S)NH-, -NHC(O)NH-, -SO₂NH-, -SONH-, phosphate, phosphonate and
4 phosphinate.

1 **25.** The composition according to claim 23, wherein each of X and Y is
2 independently selected from the group consisting of -C(O)O-, -C(O)NH-, -OC(O)NH- and
3 -NHC(O)NH-.

1 **26.** The composition according to claim 12, wherein A is N, R² is benzyl,
2 k, m and n are 1, and X is -C(O)O-.

1 **27.** The composition according to claim 13, wherein R⁴ is S, R⁵ is NHR⁶,
2 R⁶ is hydrogen, methyl, allyl, butyl or phenyl, k and m are 1 and X is -C(O)O-.

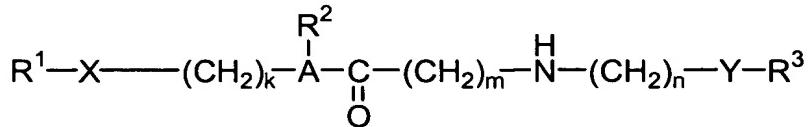
1 **28.** The composition according to claim 14, wherein R⁵ is NHR⁶, R⁶ is
2 hydrogen, methyl, allyl, butyl or phenyl, k is 2 and X is -C(O)O-.

1 **29.** The composition according to claim 15, wherein Ar is an unsubstituted
2 aryl group, R⁴ is S, R⁵ is NHR⁶, R⁶ is hydrogen, methyl, allyl, butyl or phenyl, k and m are 1
3 and X is -C(O)O-.

1 **30.** A method for increasing the transport of a biologically active
2 compound across a biological membrane comprising:
3 administering a composition comprising a biologically active compound and a
4 transport moiety, wherein the transport compound comprises a structure selected from the
5 group consisting of (ZYZ)_nZ, (ZY)_nZ, (ZYY)_nZ and (ZYYY)_nZ, wherein Z is L-arginine or
6 D-arginine, and wherein Y is an amino acid that does not comprise an amidino or guanidino
7 moiety, and wherein n is an integer ranging from 2 to 10,
8 wherein transport of the biologically active compound across the biological
9 membrane is increased relative to transport of the biologically active compound in the
10 absence of said transport moiety.

1 **31.** The method according to claim 20, wherein the biologically active
2 compound is attached to the transport moiety by a linking moiety to form a conjugate.

1 **32.** The method of claim 21, wherein the conjugate has the following
2 structure:



wherein:

5 **R**¹ is the biologically active compound ;

6 **X** is a linkage between a functional group on the biologically active compound
7 and a functional group on the linker between **R**¹ and **R**³;

8 **Y** is a linkage between a functional group on the transport moiety and a functional
9 group on the linker between **R**¹ and **R**³;

10 **A** is N or CH;

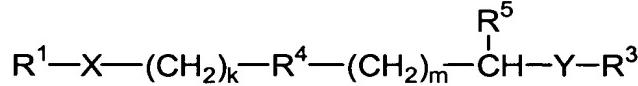
11 **R**² is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;

12 **R**³ is a transport moiety;

13 k and m are independently either 1 or 2; and

14 n is an integer of from 1 to 10.

1 **33.** The method of claim 21, wherein the conjugate has the following
2 structure:



wherein:

5 **R**¹ is the biologically active compound ;

6 **X** is a linkage between a functional group on the biologically active compound
7 and a functional group on the linker between **R**¹ and **R**³;

8 **Y** is a linkage between a functional group on the transport moiety and a functional
9 group on the linker between **R**¹ and **R**³;

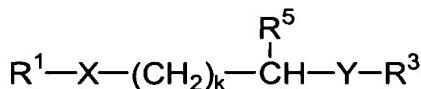
10 **R**³ is a transport moiety;

11 **R**⁴ is S, O, NR⁶ or CR⁷R⁸;

12 **R**⁵ is OH, SH or NHR⁶;

13 R⁶ is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;
14 R⁷ and R⁸ are independently hydrogen, alkyl or arylalkyl; and
15 k and m are independently either 1 or 2.

1 34. The method of claim 21, wherein the conjugate has the following
2 structure:



4 wherein:

5 R¹ is the biologically active compound;

6 X is a linkage between a functional group on the biologically active compound
7 and a functional group on the linker between R¹ and R³;

8 Y is a linkage between a functional group on the transport moiety and a functional
9 group on the linker between R¹ and R³;

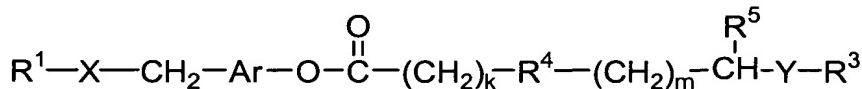
10 R³ is the transport moiety;

11 R⁵ is H, OH, SH or NHR⁶;

12 R⁶ is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl; and

13 k is 1 or 2.

1 35. The method of claim 21, wherein the conjugate is of the following
2 structure:



4 wherein:

5 R¹ is the biologically active compound;

6 X is a linkage between a functional group on the biologically active compound
7 and a functional group on the linker between R¹ and R³;

8 Y is a linkage between a functional group on the transport moiety and a functional
9 group on the linker between R¹ and R³;

10 Ar is a substituted or unsubstituted aryl group, wherein the methylene and oxygen
11 substituents are either *ortho* or *para* to one another;

12 R³ is the transport moiety;

13 R⁴ is S, O, NR⁶ or CR⁷R⁸;

14 R⁵ is H, OH, SH, CONHR⁶ or NHR⁶;

- 15 R⁶ is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;
16 R⁷ and R⁸ are independently hydrogen or alkyl; and,
17 k and m are independently either 1 or 2.